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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/265,307	03/09/1999	NIGEL L. WEBB	N0260/7031(E)	4390

7590 10/20/2004

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BOSTON, MA 02210

EXAMINER

TRINH, BA K

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/265,307

Applicant(s)

WEBB ET AL.

Examiner

Ba K. Trinh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07/14/2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1,5,7,12,17,21,23,28,33,57,62,65,69,70,75,78,82,84,89,90,94,97,101,103,107,108,110,114,119-201 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☒ Claim(s) 57,62,65,69,70,75,78,82,84,89,90,94,97,101,103,107,108,110,114,143-187 is/are allowed.
- 6) ☒ Claim(s) 1,5,7,12,17,21,23,33,119-121,123-126,128-131,134-136,139-142,188-201 is/are rejected.
- 7) ☒ Claim(s) 28,122,127,132-133,137-138 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 March 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

U.S. Patent and Trademark Office
PTO-326 (Rev. 04-01)

Office Action Summary

Part of Paper No. 31

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DETAILED ACTION

Claims 1, 5, 7, 12, 17, 21, 23, 28, 33, 57, 62, 65, 69, 70, 75, 78, 82, 84, 89, 90, 94, 97, 101, 103, 107, 108, 110, 114, 119 – 201 are pending.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5, 7, 12, 17, 21, 23, 33, 119-121, 123-126, 128-131, 134-136, 139-142, 188-201 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al, Kataoka et al and Rentsch et al.

Yoshida et al teaches an acyl derivative of arabinofuranosylcytosine (Ara-C) has better anti-leukemia than the parent; and can be used at high doses as compared to the maximum tolerance dose (MTD); note the summary and columns 1 and 2 page 1820 and Charts 1 and 2 in page 1821 of the reference. The acyl moiety contains an alkyl chain of 21 carbon atoms (or a fatty acid moiety) which is conjugated to Ara-C to form the acyl derivative (BH-AC). The initial dose was 500mg/m², and was then raised to 1,300mg/m², at which level the experiment was stopped because a rash was observed. Kataoka et al teaches that the fatty acid endows Ara-C with hydrophobicity thus enables BH-AC to be released slowly in the body and would circulate in the body for a prolonged period of time; note the Summary and the Introduction in page 147 of the reference. Rentsch et al teaches hexadecyl and octadecyl of Ara-C (C₁₆ and C₁₈ fatty acid moieties) were active at molar concentrations one-sixteenth of those of Ara-C (the parent drug void of the acyl moiety); note the third paragraph in column 2 page 1076 and Figure

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1 in page 1077 of the reference. Thus, the claimed invention would be deemed obvious over the teachings of the prior art since the addition of the fatty acid to the cancer drug (Ara-C) would enable the increase of the dosage of the conjugated drug without harming the body .The conjugated drug has lower solubility in the body fluid and is released slowly to the body, thus a higher dose can be used and tolerated as compared to the parent drug.

Applicant's response and Declaration filed on 07/20/2004 had been considered but not found persuasive. The claimed anticancer compound embraces various compounds including the compounds of the cited references and of the references in the declaration . although the prior art does not investigate the toxicity resulting from the administration of the parent drug and its conjugate, it implies that the disclosed dosages would be in the safety range unless applicant can prove otherwise. The items 10 to 12 in the Declaration do not provide any information regarding the conjugate-methotrexate since the issue herein is the fatty acid-drug conjugate and the dosage over the MTD of the drug. The item 11 is also obvious since different MTD of methotrexate are expected from the different mode of the drug administration.

Claims 57, 62, 65, 69, 70, 75, 78, 82, 84, 89, 90, 94, 97, 101, 103, 107, 108, 110, 114, 143-187 are allowable.

Claims 28, 122, 127, 132-133, 137-138 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

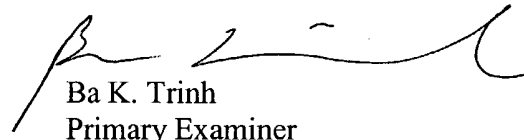
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ba K. Trinh whose telephone number is (571) 272-0695. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Ba K. Trinh
Primary Examiner
Art Unit 1625

TRINH/BKT
18 October 2004